Cancer Incidence in Danish Phenoxy Herbicide Workers, 1947–1993

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A cohort study was undertaken of 2119 workers from Denmark who were potentially exposed to phenoxy herbicides. The workers were from two factories that produced phenoxy herbicides since 1947 and 1951, respectively. They had been employed either in the manufacture of phenoxy herbicide or in the manual service functions. The main product was 4-chloro-2-methylphenoxyacetic acid (MCPA). From 1947 to 1993 the 2119 workers had a slightly lower overall cancer incidence than the Danish population (observed = 204; expected [Exp] = 234.23; standardized incidence ratio [SIR] = 0.87; 95% confidence interval [CI] 0.8–1.0). Four soft-tissue sarcoma cases were observed (Exp = 2.47; SIR = 1.62; 95% CI = 0.4–4.1). All four cases occurred among men from Kemisk Værk Køge (Exp = 1.68; SIR = 2.38; 95% CI = 0.7–6.1). There were six cases of non-Hodgkin's lymphoma (Exp = 5.07; SIR = 1.10; 95% CI = 0.4–2.6) and no significantly elevated risk of other cancers. Based on small numbers, the study suggests an association between the exposure to MCPA and related phenoxy herbicides and the risk of soft-tissue sarcoma. The study does not indicate a risk of non-Hodgkin's lymphoma after exposure to these phenoxy herbicides or a risk of other cancer diseases. — Environ Health Perspect 106(Suppl 2):683–688 (1998). http://ehpnet1.niehs.nih.gov/docs/1998/Suppl-2/683-688lynge/abstract.html

Key words: cancer incidence, Denmark, non-Hodgkin's lymphoma, phenoxy herbicide, soft-tissue sarcoma

Introduction

The dichlorophenol- and chlorocresol-based phenoxy herbicides have been manufactured since the late 1940s and have been used widely for weed control in growing grains for cereals. The phenoxy herbicides based on dichlorophenols are 2,4-dichlorophenoxyacetic acid (2,4-D), 2(2,4-dichlorophenoxy)propanoic acid (2,4-DP), and 2-(2,4-dichlorophenoxy)butyric acid (2,4-DB). Those based on chlorocresol are 4-chloro-2-methylphenoxyacetic acid (MCPA), 2-(4-chloro-2-methylphenoxy)

propanoic acid (MCPP), and 2-(4-chloro-2-methylphenoxy)butyric acid (MCPB). In Denmark, use of these phenoxy herbicides reached a maximum in 1983 with a total of 3000 tons. This is equivalent to approximately 0.6 kg/ inhabitant/year or to 31 kg/person working in farming.

One factory in Denmark, Kemisk Værk Køge, started to produce 2,4-D in 1947 and MCPA in 1949. MCPA soon became by far the predominant product, but a variety of other substances also was produced. Manufacture of MCPA was started in a second smaller factory in Denmark, Esbjerg Kemikaliefabrik, in 1951(1). Cancer incidence (2,3) and mortality (4) have been studied among the 4400 workers from these two factories from 1947 to 1987. The Danish study was set up explicitly for the study of the incidence of soft-tissue sarcoma (STS) and non-Hodgkin's lymphoma (NHL) in workers manufacturing phenoxy herbicides after the reporting of increased risks of these diseases in sprayers of phenoxy herbicides in Sweden (5,6).

The Danish cohort study of employees from the two phenoxy herbicide manufacturing plants is the only large cohort study for which cancer incidence data are available. This is particularly important for identification of STS cases. Mortality studies are less sensitive in this respect. In the *International Classification of Diseases* (7), visceral sarcomas are coded together with the carcinomas of the respective organs, and only the residual group of connective tissue sarcomas is coded as a separate entity. However, from the very beginning of cancer registration in Denmark in 1943, a locally adopted coding scheme has been applied where, for example, a carcinoma of the stomach is coded 151, but a sarcoma of the stomach is coded 851.

Materials and Methods

All persons ever employed in either of the two factories from the start of phenoxy herbicide manufacture until 1981 were included in the study. Data collection for the first analysis was carried out in 1981, and the cohort was not updated as Kemisk Værk Køge stopped the manufacture of phenoxy herbicides a few years later. Registration of employees was based on personnel files in the two factories, on public pension-scheme records from 1964 onwards, and on records kept by the company physician in Kemisk Værk Køge. Periodical industrial statistics data were used to control the completeness in identification of cohort members.

The total cohort included 4491 persons, of whom 4461 (99%) were successfully traced (3). They were followed through 1993 for death and emigration by linkage with the Central Population Register and for cancer incidence through the Danish Cancer Register.

Exposure measurement data were not available in the past and therefore had to be inferred from the available data on production. MCPA and, later, 2,4-DP and MCPP were the main products. At Kemisk Værk Køge, during the 1950s and 1970s, up to 50% of the MCPA was produced as spray-dried MCPA-sodium salt, a very fine powder. Small amounts of 2,4-D and negligible amounts of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) were produced at Kemisk Værk Køge, whereas these compounds were never produced at Esbjerg Kemikaliefabrik. At various times within the phenoxy herbicide department at Kemisk Værk Køge, limited production of aniline salts, copper thalocyanin, malein hydrazide, cetyl pyridium chloride, sodium hypochloride, and sodium acetate also took place, and purchased DDT, parathion, and dinoseb were formulated. In both factories,

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Abbreviations used: 2,4-D, 2,4-dichlorophenoxyacetic acid; 2,4-DP, 2(2,4-dichlorophenoxy)propanoic acid; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-trichlorophenol; Cl, confidence interval; Exp, expected; IARC, International Agency for Research on Cancer; MCPA, 4-chloro-2-methylphenoxyacetic acid; MCPB, 2-(4-chloro-2-methylphenoxy)butyric acid; MCPP, 2-(4-chloro-2-methylphenoxy)propanoic acid; NHL, non-Hodgkin's lymphoma; Obs, observed; SIR, standardized incidence ratio; SMR, standardized mortality ratio; STS, soft-tissue sarcoma; TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

other substances were produced in separate departments, including various dyes and pigments at Kemisk Værk Køge.

Workers in each plant were classified according to potential herbicide exposure based on their work area noted in the personnel files. Of the workers considered potentially to have been exposed to phenoxy herbicides in their work, 940 were employed in the phenoxy herbicide manufacturing and packaging departments and 1179 in manual service function. Thus, a total of 2119 workers potentially were exposed to phenoxy herbicides (Table 1).

Individual risk periods began with the beginning of phenoxy herbicide production-1947 at Kemisk Værk Køge and 1951 at Esbjerg Kemikaliefabrik, respectively—or on the date of first employment if this came later. The periods ended on the date of death or emigration or 31 December 1993, whichever came first. All tumors diagnosed during the individual risk periods were included in the analysis. Expected numbers of cancer cases were based on cancer incidence rates for the Danish population for sex, 5-year age, and calender groups. As described above, both the observed (Obs) and the expected (Exp) numbers of STSs include sarcomas topographically coded to

connective tissue as well as sarcomas topographically coded to organs. A standardized incidence ratio (SIR) was calculated by dividing the observed number of cases by the expected number. Confidence intervals (CI) for the SIRs were calculated under the assumption that the observed number of cases followed a Poisson distribution.

Results

From 1947 to 1993 the 2119 workers with potential exposure to phenoxy herbicides developed a total of four cases of STS (Exp = 2.47; SIR = 1.62; 95% CI = 0.4-4.1;90% CI = 0.6-3.7) (Table 2). All four cases occurred among men from Kemisk Værk Køge (Exp = 1.68; SIR = 2.38; 95% CI = 0.7-6.1; 90% CI = 0.8-5.5). One patient was employed in the manufacture of phenoxy herbicides and three patients were employed in the shipping department. The employment periods varied from 3 months to 21 years. The patients were all diagnosed before 1987 and thus were included in the previous analysis of the cohort (3). One case originally diagnosed with STS in 1980 had the diagnosis changed to another disease at autopsy; this case was therefore included only in the first analysis of the data for 1947 to 1982 (2).

 Table 1. Number of persons employed in the phenoxy herbicide factories in Denmark, 1947–1981, by department.

		Men	Women			
Department in factory ^a	Kemisk Værk Køge	Esbjerg Kemikalie- fabrik	Kemisk Værk Køge	Esbjerg Kemikalie- fabrik		
Manufacture and packaging						
of phenoxy herbicide	599	91	223	27		
All manual						
service functions	907	54	192	26		
Manufacture of other						
substances ^b	1077	205	94	164		
Office	160	18	235	31		
Unspecified	278	1	79	0		
Total	3021 ^c	369 ^c	823	248		

These are in hierarchic order for persons who were employed in more than one department. This is a heterogeneous group. The largest subgroup was employed in the manufacture of various organic and inorganic dyes and pigments at Kemisk Værk Køge. One person with employment periods in both factories is included in both populations.

Two cases of STS occurred among men from Kemisk Værk Køge from departments not potentially exposed to phenoxy herbicides; one patient was employed in pigment milling and one patient in administration. The STS cases are listed in Table 3.

Persons potentially exposed to phenoxy herbicide had an incidence of NHL close to that of the Danish population (Obs = 6; Exp = 5.07; SIR = 1.10; 95% CI = 0.4–2.6) (Table 2). For completeness, it should be added that 10 NHL cases occurred among persons from Kemisk Værk Køge from departments not potentially exposed to phenoxy herbicides; this represents a clear excess risk but is not relevant for the present study.

The 2119 workers with potential exposure to phenoxy herbicides had a slightly lower overall cancer incidence than the Danish population (Obs = 204; Exp = 234.23; SIR = 0.87; 95% CI = 0.8–1.0) (Table 4).

Table 4 also lists observed and expected cancer cases by the diagnostic groups traditionally used in cancer epidemiology (8). Only cancer sites with at least two observed cases in either men or women are included in the table. The viseral sarcomas are here, according to the traditional classification, are included in the respective organ groups. No statistically significant excess risks were found. At the borderline of statistical significance were an SIR of 1.92 for cervical cancer (95% CI = 0.9-3.6) and an SIR of 1.41 for rectal cancer in men (95% CI = 0.8-2.4). An SIR of 2.24 for bladder cancer in women was found based on three cases, and an SIR of 4.55 for multiple myeloma in women based on two cases.

Discussion

Results of this updated analysis of the cancer incidence in the Danish cohort support the results of the previous analysis (2,3). The Danish study indicates that work in the manufacture of MCPA, MCPP, and 2,4-DP does not influence the

Table 2. Observed and expected number of soft-tissue sarcoma and non-Hodgkin's lymphoma, 1947–1993, among 2119 workers potentially exposed to phenoxy herbicide factories in two Danish factories.

	Kemisk Værk Køge				Esbjerg Kem	nikaliefabrik	Total			
	Obs	Ехр	SIR	95% CI	Obs	Ехр	Obs	Ехр	SIR	95% CI
Soft-tissue sarcoma										
Men	4	1.68	2.38	0.7-6.1	0	0.16	4	1.84	2.18	0.6-5.6
Women	0	0.58	_	_	0	0.05	0	0.63		
Total	4	2.26	1.77	0.5-4.5	0	0.21	4	2.47	1.62	0.4-4.1
Non-Hodgkin's lymphoma										
Men	5	3.72	1.34	0.4-3.1	0	0.37	5	4.09	1.22	0.4-2.9
Women	1	0.92	1.09	0.03-6.1	Ö	0.06	1	0.98	1.02	0.03-5.7
Total	6	4.64	1.29	0.5-2.8	Ō	0.43	6	5.07	1.10	0.4-2.6

Table 3. Soft-tissue sarcoma patients among persons employed at Kemisk Værk Køge, Denmark.

Sex	Approximate age ^a at diagnosis	Approximate years ^a of diagnosis	Cancer register diagnosis	Final histology diagnosis	Cause of death (<i>ICD-8</i>) ^b	Factory department	Duration of employment	Years since first employed
Soft-t Man	tissue sarcoma 50	cases with pot 1970	ential exposure to pheno Dermatofibro- sarcoma; back	ky herbicides, 1947—1993 Hemangioperi- cytoma; back	Malignant neoplasm of unspecified origin (195.9)	Shipping	7 years	21
Man	25	1975	Fibrosarcoma; lower limb	Neurofibrosarcoma; lower limb	Malignant neoplasms of connective tissue in lower limb (171.3)	Shipping	3 months	5
Man	65	1975	Leiomyosarcoma; prostate	Leiomyosarcoma; prostate, wall of bladder or vessel	Malignant neoplasms of prostate (185.x)	Shipping	2.5 years	17
Man	75	1985	Angiosarcoma Karposi; foot	Angiosarcoma Karposi; foot	Chronic ischemic heart disease (412.9)	Manufacture of black pigments Manufacture of phenoxy herbicides	3 years 21 years	29 ^c
Previo Man	ous soft-tissue 35	sarcoma case v 1980	vith potential exposure to Sarcoma; retro- peritoneum	o phenoxy herbicides, include Alive Mesenchymal tumor (possible liposarcoma); retroperitoneum Postmortem Malignant histiocytosis	d only in the analysis, 1947- Hemorrhage, brain (431.9)	-1982 Phenoxy herbicide packaging	3 months	14
Soft-t Man	tissue sarcoma 55	cases without 1980	potential exposure to phe Mesenchymal tumor; larynx	enoxy herbicides, 1947–1993 Leiomyosarcoma; larynx	Malignant neoplasms of larynx (161.9)	Pigment milling	0.5 months	26
Man	81	1990	Malignant histio- cytoma; skin of leg	NA	Malignant neoplasms of ill-defined sites, other (195.9)	Administration	21 years	37

NA, not applicable. For reasons of confidentiality only approximate age and year are provided. World Health Organization (7). Phenoxy herbicide department from start of employment.

Table 4. Observed and expected incident of cancer cases, 1947–1993, among 2119 workers potentially exposed to phenoxy herbicides in two Danish factories.

ICD-7			N	len		Women				
	Site ^a	Obs	Ехр	SIR	95% CI	Obs	Ехр	SIR	95% CI	
140-205	All malignant									
	neoplasms	158	176.63	0.89	0.8-1.0	46	57.60	0.80	0.6-1.1	
150	Esophagus	2	2.23	0.90	0.1-3.2	0	0.23	_	_	
151	Stomach	8	7.78	1.03	0.4-2.0	1	1.15	0.87	0.02-4.8	
153	Colon including									
	rectosigmoid	12	11.70	1.03	0.5-1.8	1	3.91	0.26	0.01-1.4	
154	Rectum, excluding	. –								
	anus	13	9.22	1.41	0.8-2.4	0	1.93	_		
157	Pancreas	4	5.09	0.79	0.2-2.0	Ō	1.26			
161	Larynx	4	3.16	1.27	0.3-3.2	Ö	0.21	_	_	
162	Lung primary,	•	0.10		0.0 0.2	•	·			
102	trachea	30	32.12	0.93	0.6-1.3	6	4.04	1.49	0.5-3.2	
170	Breast	Ö	0.28			12	14.18	0.85	0.4-1.5	
171	Cervix uteri	_		_		9	4.68	1.92	0.9-3.6	
177	Prostate	15 ^b	14.99	1.00	0.6-1.7	_			-	
178	Testis	4	4.30	0.93	0.3-2.4	_		_		
180	Kidney	2	5.69	0.35	0.04-1.3	0	1.25	_	****	
181	Urinary bladder	2	5.05	0.00	0.04 1.0	Ū	1.20			
101	including papilloma	12	14.59	0.82	0.4-1.4	3	1.34	2.24	0.5-6.5	
190	Melanoma of skin	5	4.05	1.23	0.4-2.9	ŏ	1.80		0.0 0.0	
191	Other skin	22 ^c	23.80	0.92	0.6-1.4	4	6.09	0.66	0.2-1.7	
198	Metastasis	3	2.52	1.19	0.2-3.5	õ	0.70	U.UU	U.Z 1.7	
199	Other and	3	2.32	1.15	0.2 0.0	Ū	0.70			
133	unspecified sites	2	1.47	1.36	0.2-4.9	1	0.50	2.00	0.05-11.1	
200, 202	Non-Hodgkin's	2	1.47	1.50	0.2 4.0	•	0.00	2.00	0.00 11.1	
200, 202	lymphoma	4	4.09	0.98	0.3-2.5	1	0.98	1.02	0.03-5.7	
203	Multiple myeloma	Õ	1.89		-	ż	0.44	4.55	0.6-16.4	
203	Leukemia	6	4.80	1.25	0.5-2.7	ī	0.97	1.02	0.03-5.7	

^{—,} not relevant. The table includes only cancer sites with at least two observed cases in either men or women. Includes one sarcoma case. Includes two sarcoma cases.

Table 5. Studies on exposure to phenoxy herbicides and the risk of soft tissue sarcoma and non-Hodgkin's lymphoma. Nonmilitary work only.

		Soft-tis	sue sarcoma	3	Non-Ho			
tudy opulation	Exposure	Number of exposed cases	RR estimate	95% CI	Number of exposed cases	RR estimate	95% CI	Reference
Nanufacture and spraying								
of phenoxy herbicides		_						
IARC register	Potential TCDD exposure	6	2.03	(0.75-4.43)	24	1.39	(0.89–2.06)	(9)
IARC register	No potential TCDD exposure	2	1.35	(0.16–4.88)	9	1.00	(0.46–1.90)	(9)
Manufacture of phenoxy herbicides								
BASF, Germany	TCDD exposure at accident	0	_	_	0	_		(20)
Dow Chemicals, US	2,4-D manufacture	0			2	3.91	(0.44–14.11)	(21)
Spraying of phenoxy herbicides								
Railway sprayers, Sweden	PH	0			0			(22)
Forest sprayers, Sweden	PH	0	_	_	0		_	(23)
Licenced sprayers, Sweden	PH	7	0.9	(0.4–1.9)	21	1.01	(0.63-1.54)	STS data (24
								NHL data (25
Public sprayers, Finland	PH	0	_	_	1	0.35	(0.01–1.97)	(<i>26</i>)
Gardeners, Denmark	PH	3	4.55	(0.94–13.3)	8	2.00	(0.86-3.93)	(<i>27</i>)
Licenced sprayers,								
The Netherlands	PH	0		_	0	_	_	(28)
Sweden, northern ^a	PH and/or chlorophenols	See below			61	6.0	(3.7–9.7)	(6)
	PH only	See below			41	4.8	(2. 9– 8.1)	
	Chlorophenols only	See below			25	8.4	(4.2–16.9)	
Sweden, middle	PH only	See below			6	4.9	(1.3–18) ^b	(13)
Sweden, southern	PH only	See below			NA	1.3	(0.8–2.1)	(16)
Sweden, meta-analysis	PH and/or chlorophenols	90	2.8	(2.1–4.4)	See above			(10)
	PH only	59	2.7	(1. 9–4 .7)	See above			
	PH > 24 days	40	3.7	(2.4–7.8)	See above			
	2,4,5-T	46	3.5	(2.3–6.7)	See above			
	2,4-D only	5	1.4	(0.4–5.1)	See above			
	MCPA only	8	1.6	(0.6–5.3)	See above			
Sweden, middle farmers,	PH	28	1.5	(0.7–3.0) ^b	NA	NA	NA	(29)
forestry gardeners		6	4.4	(1.0–18) ^b	NA	NA	NA	
New Zealand	PH	17	1.6	(0.7–3.3) ^b	29	1.0	(0.6–1.5) ^b	STS data (30
	Chlorophenols	8	1.5	(0.5–4.5) ^b	20	1.3	(0.8–2.3) ^b	NHL data (3
Kansas	PH	22	0.9	(0.5–1.6)	40	1.6	(0.9–2.6)	(14)
	PH ≥21 d/y	NA	NA	NA	7	6.0	(1.9–19.5)	
Nebraska								
Men	PH	NA	NA	NA	43	1.5	(0.9–2.5)	(15)
	2,4,5-T	NA	NA	NA	13	1.6	(0.7–3.6)	
	2,4-D only	NA	NA	NA	NA	1.5	(0.8–2.6)	
	PH ≥21 d/y	NA	NA	NA	3	3.3	(0.5–22.1)	
Women	PH	NA	NA	NA	2	0.9	(0.1–4.5)	(32)
lowa and Minnesota	PH	NA	NA	NA	118	1.2	(0.9–1.6)	(17)
	2,4,5-T	NA	NA	NA	25	1.2	(0.7–1.9)	
	2,4-D	NA	NA	NA	115	1.2	(0.9–1.6)	
Washington State	PH, high use	NA	0.89	(0.4–1.9)	NA	1.24	(0.8–1.9)	(33)
	chlorophenols, high use	NA	0.93	(0.5–1.8)	NA	0.92	(0.9–1.4)	
Saskatchewan, Canada								
Farmers, 250 acres								
sprayed	PH	NA	NA	NA	15	1.34	(0.74–2.38)	(34)
As above and	8.1	• • •				a :=		
farm was < 1000 acres	PH	NA	NA	NA	NA	2.17	(1.02–4.62)	
Italy	2,4,5-T	4	2.70	(0.6–12.4)	NA	NA	NA	(11)
England and Wales farmers	PH	9	1.15	(0.83–1.59)	NA	NA	NA	(35)
Environmental exposure to								
TCDD, chlorophenols, etc.								
Seveso	TCDD in air							(12)
	Zone A	0	_	_	0	-		
	Zone B	0	_		4	1.7	(0.5–4.3)	
** 1	Zone R	. 8	2.4	(1.0-4.5)	22	1.3	(0.8–1.9)	(00)
inland, southern	Chlorophenols in tap water	NA	8.9	(1.8–44)	NA	2.8	(1.4–5.6)	(<i>36</i>)
Novara and Vercelli, Italy Men	2,4-D and 2,4,5-TP	NA	NA	NA	NA	2.2	(1.4–3.5)	(37)

Abbreviations: NA, not available; PH, phenoxy herbicides; RR, relative risk. Data listed under NHL include all malignant lymphomas. 90% confidence interval.

overall risk of cancer. This is in accordance with the result of the International Agency for Research on Cancer (IARC) multicenter study, in which the overall cancer mortality among persons exposed to phenoxy herbicides not potentially contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) was equal to that of their national populations (9). The Danish cohort formed part of the IARC study.

Based on small numbers, the Danish study continues to suggest an association between exposure to MCPA, MCPP, and 2,4-DP and risk of STS. There is now quite a strong indication of an association between potential exposure to 2,4,5-T and/or TCDD and risk of STS. The evidence comes from the IARC multicenter study (9), the meta-analysis of the Swedish case-control studies (10), an Italian case-control study (11), and from the Seveso data (12) (Table 5). The overall evidence, on the other hand, is much weaker for an association between exposure to other phenoxy herbicides and risk of STS. For phenoxy herbicides not likely contaminated with TCDD, the IARC multicenter study showed an standardized mortality ratio (SMR) of 1.35 (Obs = 2, where one death came from Denmark); for MCPA and 2,4-D, the Swedish meta-analysis showed relative risks of 1.6 (95% CI = 0.6-5.3) and 1.4 (95% CI = 0.4-5.1), respectively (Table 5).

It is clear that the suggested excess risk of STS in the Danish cohort study was detected only because the national cancer incidence data from the very beginning of registration in 1943 included separate codes for visceral sarcomas. Only one of the four visceral sarcoma patients had a sarcoma topographically coded to the connective tissue. The sensitivity of epidemiologic studies on STS thus depends highly on the data source, and the Danish coding scheme ensures that all STSs are identified.

The study does not support an association between phenoxy herbicide exposure and subsequent risk of NHL. At present, the findings from various studies on the risk of NHL following exposure to phenoxy herbicides are equivocal. Excess risks were indicated in some Swedish (6,13) and American (14,15) case—control studies but not in all (16,17). In the IARC multicenter study (19) and in the Seveso data (12) the risks are slightly but statistically nonsignificantly elevated among persons with potential exposure to TCDD, whereas the risk was not elevated in the IARC study population without potential exposure to TCDD.

The borderline excess risk of cervical cancer in the present study is unexplained. Women with potential exposure to phenoxy herbicides worked mainly in the packaging and cleaning areas. Packaging was seasonal work and the workers came mainly from surrounding rural areas. Women who farm in Denmark, however, have a deficit risk of cervical cancer (18). Two cases of multiple myeloma occurred among women in the study. Although there are some

indications in the literature for a possible association between exposure to phenoxy herbicides and multiple myeloma (19), the literature is not consistent. It therefore seems prudent not to overinterpret the finding of an excess risk in the Danish study based on only two cases.

When data were collected for the present study, considerable efforts were made to ensure a complete assertainment of the cohort members, using both personnel files and files kept by the company doctors, public pension scheme data, and data from the periodical industrial statistics (1). No healthy worker effect was apparent in the cohort, in which the overall mortality during the first 35 years of follow-up was close to that of the Danish population (4). Cohort members from the phenoxy herbicide departments were exposed predominantly but not exclusively to phenoxy herbicides, but none of the other exposures that occurred in the phenoxy herbicide departments are known to be clearly related to a risk of STS.

Based on the foregoing data, it may be concluded that this Danish study indicates that work in the manufacture of MCPA, MCPP, and 2,4-DP does not increase the overall risk of cancer. Based on small numbers, this very sensitive Danish study continues to suggest an association between exposure to these phenoxy herbicides and risk of STS. The study does not support an association between phenoxy herbicide exposure and risk of NHL.

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